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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,622	05/07/2002	Nicholas Bachynsky	HO-P01615WO0	1907

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EXAMINER	
ROYDS, LESLIE A	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 11/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,622	BACHYNSKY ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2006; 06 July 2006;31 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *100,101 and 103-121* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *100-109,111-117 and 119-121* is/are rejected.

7)☒ Claim(s) *110 and 118* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/28/06;08/14/06;08/29/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 100-101 and 103-121 are presented for examination.

A request for continued examination under 37 C.F.R. 1.114, including the fee set forth in 37 C.F.R. 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. 1.114, and the fee set forth in 37 C.F.R. 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 C.F.R. 1.114. Applicant's payment and request filed May 25, 2006 have been received and entered into the present application. Accordingly, prosecution has been reopened.

Applicant's response filed July 6, 2006 in response to the Notice of Non-Compliant Amendment dated June 6, 2006 has also been received and entered into the application. Additionally, Applicant's Supplemental Amendment filed August 31, 2006, in response to the Interview held August 17, 2006, has also been received and entered into the application.

Applicant's Information Disclosure Statements (IDS) filed April 28, 2006 (two pages), August 14, 2006 (one page) and August 29, 2006 (one page) have each been received and entered into the present application. As reflected by the attached, completed copies of form PTO/SB/08A (four pages total), the Examiner has considered the cited references except for the references cited as B1 and C28 on the IDS dated April 28, 2006. A reasonable search by the Examiner did not locate the references in the record. Accordingly, they have not been considered.

Claims 100-101 and 103-121 are pending and are under examination. Claim 102 has been cancelled and claims 100, 109 and 116 are amended.

Applicant's arguments, filed July 6, 2006, have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Objections to the Claims (New Grounds of Objection)

Claim 107 is objected to because the word "methotrexate" is misspelled as "metholtrexate" at line 2 of the claim.

Claims 100, 109 and 116 are objected to for reciting, "comprising the step of administering an amount of a mitochondrial uncoupling agent sufficient to the subject to induce whole body intracellular hyperthermia in the subject", which is grammatically awkward. Applicant may wish to consider amending the claims to read ---comprising the step of administering to the subject an amount of a mitochondrial uncoupling agent sufficient ~~to the subject~~ to induce whole body intracellular hyperthermia in the subject---.

Claims 110 and 118 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description Requirement

(New Grounds of Rejection)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 100, 103-109, 111-117 and 119-121 are rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement. The claim contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Present claims 100, 109 and 116 and the claims dependent therefrom are directed to a method for inducing intracellular hyperthermia in a subject comprising the step of administering an amount of a

mitochondrial uncoupling agent sufficient to induce whole body intracellular hyperthermia in the subject, wherein the hyperthermia is used to treat cancers (i.e., prostate carcinoma, glioblastoma multiforme, Kaposi's sarcoma, peritoneal carcinoma or glioma), infections (i.e., Borrelia burgdorferi, Mycobacterium leprae, Treponema pallidum, HIV, hepatitis C, herpes virus or papillomavirus) or infestations (i.e., Candida, Sporothrix schenkii, Histoplasma, Paracoccidiodes, Aspergillus, Leishmania, malaria, acanthomoeba or cestodes). Present claims 103, 111 and 119 specify that the mitochondrial uncoupling agent is a conjugate of 2,4-dinitrophenol.

In particular, the specification as originally filed fails to provide adequate written description for the claim limitations directed to (1) a mitochondrial uncoupling agent (claims 100, 109 and 116) or (2) a conjugate comprising 2,4-dinitrophenol (claims 103, 111 and 119).

Regarding the requirement for adequate written description of chemical entities, Applicant's attention is directed to the MPEP §2163. In particular, *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plain for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for *Examination of Patent Applications* under the 35 U.S.C. 112.1 "Written Description" Requirement ("*Guidelines*"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics when coupled with a known or disclosed correlation between function and structure..." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 316, 1324-25 (Fed. Cir. 2002) (quoting *Guidelines*, 66 Fed. Reg. at 1106 (emphasis added)). Moreover, although *Eli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in

general. *Univ. of Rochester v. G.D. Searle & Co.*, 249 Supp. 2d 216, 225 (W.D.N.Y. 2003).

Present claims 100, 109 and 116 and the claims dependent therefrom recite the use of a "mitochondrial uncoupling agent" to induce intracellular hyperthermia. However, Applicant has failed to provide sufficient written description to support the genus of "mitochondrial uncoupling agents". In fact, the present disclosure fails to recite any structural characteristics, chemical formula or physical properties that correlate to the compound's function as a mitochondrial uncoupler that would provide adequate and limiting description of the mitochondrial uncoupling agents that Applicant was actually in possession of, and intended to be used within the context of the present invention, at the time of the present invention.

Despite the fact that Applicant provides lists of compounds that are either "classic" uncoupling agents (i.e., those that act similarly to DNP), ionophorous antibiotics or a group of "heterogeneous compounds that dissipate the proton gradient by attaching or interacting with specific proteins in the inner mitochondrial membrane" (see pages 25-27 of the present specification), the lists are exemplary and fail to provide a limiting definition or any structural, chemical or physical characteristics of the mitochondrial uncoupling agents such that one of ordinary skill in the art would have been able to readily identify the scope of those compounds encompassed by the term "mitochondrial uncoupling agents".

Although Applicant states that the mitochondrial uncoupling agents are capable of increasing intracellular heat and freeing radicals (see page 14 of the specification), such properties do not clearly and precisely point out those mitochondrial uncouplers of which Applicant was in possession at the time of the invention. While it may be construed that the fact that the agent must be capable of the function of mitochondrial uncoupling is sufficient to fulfill the written description requirement of 35 U.S.C. 112, first paragraph, Applicant has failed to tie this functional property of the exemplary disclosed compounds to some sort of chemical or physical structure such that one of skill in the art would have been able to readily identify the compounds intended to be encompassed by the claims. In other words, the absence of any correlation between function and physical or chemical structure fails to provide an adequate

description of the entire genus of compounds that fall within the genus of mitochondrial uncouplers. Furthermore, given the great variation in chemical structure, function and physical properties between each of the exemplified uncouplers present in the specification, one of skill in the art would have required additional direction and/or description as to what other compounds would be considered mitochondrial uncouplers, how such agents could be readily identified and whether such uncouplers would have been amenable for use in the claimed invention. In the absence of such description, Applicant's limitation to a "mitochondrial uncoupling agent" is not sufficiently supported by the present specification in such a way as to satisfy the written description requirement of 35 U.S.C. 112, first paragraph.

Regarding Applicant's limitation directed to "a conjugate of 2,4-dinitrophenol" (claims 103, 111 or 119), Applicant has failed to provide any structural characteristics, chemical formula, name(s) or physical properties that would provide adequate written description of the 2,4-dinitrophenol conjugates that Applicant was actually in possession of, and intended to be used within the context of the present invention, at the time of the present invention.

Applicant's specification states, "Various conjugates, adducts, analogs and derivatives of the above mentioned agents can be formulated and synthesized to enhance intracellular uncoupling and heat production...Uncoupling-free radical prodrug compounds may thus exert greater selective killing of transformed cells by undergoing a higher flux of reduction or electron acceptance in tumor cells. In this regard, the contents of U.S. Patent NO. 5,428,163 and the published methods of C-alkylation of phenols and their derivatives by Hudgens, T.L. and Turnbull, K.D. are hereby incorporated by reference."

Such disclosure, while noted, provides only an exemplary and non-limiting teaching of what compounds would be considered within the scope of the term "conjugate of 2,4-dinitrophenol". Applicant has failed to provide any limiting definition or any structural, chemical or physical characteristics of these conjugate compounds such that one of ordinary skill in the art would have been able to readily identify the scope of those compounds encompassed by the term "a conjugate of 2,4-

dinitrophenol".

While it may be construed that the fact that the compound is derived from or based upon the compound 2,4-dinitrophenol implies some sort of chemical or structural characteristic sufficient to fulfill the written description of 35 U.S.C. 112, first paragraph, it is herein noted that Applicant has failed to describe in any certain terms the degree of derivation or similarity that a compound may have from the parent compound 2,4-dinitrophenol and still be considered a conjugate for use as the mitochondrial uncoupling agent to induce intracellular hyperthermia. The mere fact that the only chemical or structural characteristic of the compound is that it is a conjugate of 2,4-dinitrophenol, wherein the degree of similarity or derivation from 2,4-dinitrophenol is herein undefined in the accompanying specification, is not sufficient to provide an adequate description of the genus of compounds intended by Applicant for use in the present invention. In the absence of such description, Applicant's limitation to "a conjugate of 2,4-dinitrophenol" is not sufficiently supported by the present disclosure in such a way as to satisfy the written description requirement of 35 U.S.C. 112, first paragraph.

Considering the teachings provided in the specification as originally filed, Applicant has failed to provide the necessary teachings, by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams and formula that fully set forth the claimed invention, in such a way as to reasonably convey to one skilled in the relevant art that Applicant had possession of (1) the genus of mitochondrial uncoupling agents or (2) conjugates of 2,4-dinitrophenol.

Accordingly, the claims are considered to lack sufficient written description and are properly rejected under 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 112, Second Paragraph (New Grounds of Rejection)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 104-105, 112 and 120 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claims 104, 112 and 120 are directed to a method for inducing intracellular hyperthermia for the treatment of, respectively, cancers (i.e., prostate carcinoma, glioblastoma multiforme, Kaposi's sarcoma, peritoneal carcinoma or glioma), infections (i.e., Borrelia burgdorferi, Mycobacterium leprae, Treponema pallidum, HIV, hepatitis C, herpes virus or papillomavirus) or infestations (i.e., Candida, Sporothrix schenkii, Histoplasma, Paracoccidiodes, Aspergillus, Leishmania, malaria, acanthomoeba or cestodes), wherein an animal is administered the mitochondrial uncoupling agent and a separate medication, wherein the second medication increases the overall metabolic rate of the animal, the metabolic rate of a specific target tissue in the animal or an increase in free radical flux.

First, it is unclear how the limitation "an animal" is intended to limit the parent claim from which it depends because each of independent claims 100, 109 or 116 recite the induction of intracellular hyperthermia in a subject. In other words, it is unclear whether the "an animal" is intended to be the same "subject" as presented in the independent claim, or whether it is intended to further limit the "subject" of the independent claim only to "an animal". Accordingly, the host intended to receive the intracellular hyperthermia cannot be readily identified by the claims as presently written and, therefore, the skilled artisan would not have been reasonably apprised of the scope of the subject matter for which Applicant is seeking protection.

Second, present claims 104, 112 and 120 require the administration of a separate medication with the mitochondrial uncoupling agent, but then state "wherein the second medication increases the overall metabolic rate of the animal, the metabolic rate of a specific target tissue in the animal or an increase in free radical flux". It is unclear whether "the second medication" is the same as the "a separate medication" referenced earlier in the claim or whether "the second medication" and the "a separate

medication" are two distinct chemical entities. Accordingly, one of ordinary skill in the art would not have been reasonably apprised of the metes and bounds of the claimed subject matter.

Third, the limitation "the metabolic rate of a specific target tissue in the animal" does not clearly or expressly delineate what "target tissue" is affected by the second medication such that the skilled artisan would have been able to readily determine those medications that would have been included or excluded from the claim based upon this required function. Accordingly, one of ordinary skill in the art would not have been reasonably apprised of the scope of the subject matter for which Applicant is seeking protection.

For these reasons, the claims fail to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and are, thus, properly rejected.

Claims 105, 107, 115 and 117 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

In particular, it is noted that the claims recite the agents "methylene blue (tetramethylthionine)", "etoposide (VP-16)", "teniposide (VM-26)", "vidarabine (ARA-A)", "9-1,3-dihydroxy-2-propoxymethylguanine (DHPG)", "2,3-dideoxytidine (ddQ)", "iododeoxyuridine (IDU)", "trifluorothymidine (TIFT)", "dideoxyMosine (ddi)", "fluconazole (Diflucan)" or "5 fluro-cytosine (Flutocytosine, 5-FC)". The recitation of the parenthetical limitation(s) renders the scope of the claims indefinite because Applicant has failed to delineate how such limitations are intended to limit the claim. Though the limitations provided in the parentheses may be additional names that circumscribe the same compound, it is unclear whether the parenthetical recitation of these terms is intended to simply make reference to another known name for that same compound, or whether it is intended to limit the claim in another manner.

For these reasons, the claims fail to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and, thus, are properly rejected because the skilled artisan would not have been reasonably apprised of the scope of the claims.

Claim Rejections - 35 USC § 102 (New Grounds of Rejection)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 100, 101, 104, 105 and 106 are rejected under 35 U.S.C. 102(b) as being anticipated by Cone Jr. (U.S. Patent No. 4,724,234; 1988).

Cone Jr. teaches a method of producing oncolysis, i.e., lysis or degeneration or death of malignant cancer cells, by concurrent administration of two therapeutic regimens, wherein the first regimen is a defined nutritional regimen to minimize the use of amino acids and fatty acids as an energy source for ATP synthesis within the cancer cell(s), and further wherein the second regimen in the administration of 2,4-dinitrophenol in an amount sufficient to uncouple oxidative phosphorylation (col.7, line 51-co..8, line 5 and col.19, lines 26-39). Cone Jr. teaches the inclusion of the essential fatty acids linoleic and linolenic acids as part of the defined nutritional regimen (col.12, lines 8-19) and exemplifies the use of the disclosed regimen in patient(s) with retroperitoneal tumor mass (Example 3, col.28-31) and adenocarcinoma of the prostate (Example 4, col.31-34).

Though Cone Jr. does not expressly teach an intracellular hyperthermic effect via the induction of heat shock proteins as a result of the disclosed regimen, the administration of the same compound as claimed (i.e., 2,4-dinitrophenol with concurrent polyunsaturated fatty acids linoleic or linolenic acid) to cancerous cells (i.e., retroperitoneal or prostate) is considered to inherently have the claimed intracellular

hyperthermic effect via the induction of heat shock proteins, whether expressly recognized by Cone Jr. or not. Products of identical chemical composition cannot exert mutually exclusive properties when administered under the same circumstances or, in the present case, the same host. Please reference MPEP §2112.

The explanation of an effect obtained when using a compound cannot confer novelty on a known process if the skilled artisan was already aware of the occurrence of the desired therapeutic effect. In other words, even if the intracellular hyperthermic effect via the induction of heat shock proteins was not itself recognized as a pharmacological effect of administering the 2,4-dinitrophenol in combination with a polyunsaturated fatty acid of Cone Jr. to patients suffering from retroperitoneal or prostate cancer, such an effect is not considered a new therapeutic application because the known treatment of retroperitoneal or prostate cancer using this combination of active agents was already known in the prior art. Though mechanisms of action of chemical entities are no doubt important contributions to scientific and pharmaceutical development, the assessment of patentability under 35 U.S.C. 102 is based upon the therapeutic applications and effects of the compounds, not the mechanism by which they exert such a therapeutic effect. Furthermore, it is generally well settled in the courts that a mechanistic property of a chemical compound, or combination of chemical compounds, when administered under identical conditions, is necessarily present, despite the fact that is may not have been readily apparent to, or recognized by, one of ordinary skill in the art.

Claim Rejections - 35 USC § 103 (New Grounds of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 100-101 and 104-108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cone Jr. (U.S. Patent No. 4,724,234; 1988) in view of Pilepich et al. ("Androgen Deprivation with Radiation Therapy Compared with Radiation Therapy Alone for Locally Advanced Prostatic Carcinoma: A Randomized Comparative Trial of the Radiation Therapy Oncology Group", *Urology*, 45(4);.1995).

Cone Jr. teaches a method of producing oncolysis, i.e., lysis or degeneration or death of malignant cancer cells, by concurrent administration of two therapeutic regimens, wherein the first regimen is a defined nutritional regimen to minimize the use of amino acids and fatty acids as an energy source for ATP synthesis within the cancer cell(s), and further wherein the second regimen in the administration of 2,4-dinitrophenol in an amount sufficient to uncouple oxidative phosphorylation (col.7, line 51-co..8, line 5 and col.19, lines 26-39). Cone Jr. teaches the inclusion of the essential fatty acids linoleic and linolenic acids as part of the defined nutritional regimen (col.12, lines 8-19) and exemplifies the use of the disclosed regimen in patient(s) with retroperitoneal tumor mass (Example 3, col.28-31) and adenocarcinoma of the prostate (Example 4, col.31-34).

Though Cone Jr. does not expressly teach an intracellular hyperthermic effect via the induction of heat shock proteins as a result of the disclosed regimen, the administration of the same compound as claimed (i.e., 2,4-dinitrophenol with concurrent polyunsaturated fatty acids linoleic or linolenic acid) to cancerous cells (i.e., retroperitoneal or prostate) is considered to inherently have the claimed intracellular

hyperthermic effect via the induction of heat shock proteins, whether expressly recognized by Cone Jr. or not. Products of identical chemical composition cannot exert mutually exclusive properties when administered under the same circumstances or, in the present case, the same host. Please reference MPEP §2112.

Though Cone Jr. does not expressly disclose the concomitant administration of an additional anticancer agent and/or radiation with the disclosed 2,4-dinitrophenol regimen, Pilepich et al. provides teachings that the administration of androgen deprivation therapy, using a combination chemotherapeutics such as goserelin and flutamide, before and during radiotherapy results in a marked increase in local control and disease-free survival of prostatic cancer patients compared with pelvic radiotherapy alone (see abstract at page 616).

One having ordinary skill in the art at the time of the present invention would have found it *prima facie* obvious to modify the method(s) disclosed by Cone Jr. to include concomitant administration of an additional anticancer agent (e.g, goserelin/flutamide) in addition to radiotherapy because each was known to have the same antitumor effects in prostate cancer patients. The very fact that each was known in the art to have the same therapeutic utility raises the reasonable expectation of success that such therapeutic modalities, when combined, would have, at minimum, additive, if not synergistic, antiproliferative effects when combined. Furthermore, the use of multiple therapeutic approaches (i.e., both chemotherapeutic and radiotherapeutic regimens) would have been reasonably expected to accommodate for the deficiencies in efficacy of single therapeutic modalities alone.

As stated in *In re Kerkhoven*, 626 F.2d 846, 205 USPQ 1069, at page 1072 (CCPA 1980): "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. *In re Susi*, 58 CCPA 1074, 1079-80, 440 F.2d 442, 445, 169 USPQ 423, 426 (1971); *In re Crockett*, 47 CCPA 1018, 1020-21, 279 F.2d 274, 276-77, 126 USPQ 186, 188 (CCPA 1960)."

Conclusion

Applicant is invited to contact the undersigned Examiner to discuss the language of the claims and the rejections of record should Applicant feel that such an interview will help advance prosecution of the present application and clarify the issues set forth *supra*.

Rejection of claims 100-109, 111-117 and 119-121 is proper.

Claims 110 and 118 are objected to as being dependent upon a rejected base claim.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leslie A. Royds
Patent Examiner
Art Unit 1614

November 8, 2006

Ardin H. Marschel 11/12/06
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER